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PRINCIPAL INVESTIGATOR: Colm Morrissey

CONTRACTING ORGANIZATION: University of Washington
Seattle, WA 98195

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14. ABSTRACT The Genitourinary Cancer Biorepository at the University of Washington joined the Prostate Cancer Pathology Resource Network (PCBN) September 30 th 2014. The purpose of this interaction is to provide high quality, well annotated specimens that can be used by prostate cancer researchers through the PCBN. The University of Washington Biorepository has a focus on advanced stage disease. Specimens provided by the University of Washington site includes blood (serum, plasma, and buffy coat), prostatectomy tissues (frozen), biopsies and metastatic tissue from rapid autopsies (paraffin embedded material and tissue microarrays (TMAs)), prostate cancer patient derived xenografts (PDX) and derived specimens (DNA and RNA) from prostate cancer patients. These specimens are linked to clinical and outcome data and supported by an informatics infrastructure. In this 2 nd year of operation the University of Washington site has accrued new specimens from the clinic, surgery, and at autopsy, manufactured and provided TMAs, sera and derived RNA and DNA where required. Specimens were made available to prostate cancer researchers through the PCBN.					
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Introduction

The Prostate Cancer Biorepository Network (PCBN) is a public bioresource that provides high quality, well annotated specimens that can be used by prostate cancer researchers through the PCBN <http://prostatebiorepository.org>. This biorepository is a collaborative effort between Johns Hopkins University (JHU), New York University (NYU), Memorial Sloan Kettering Cancer Center (MSKCC), University of Washington (UW), Washington University (WU), and the Department of Defense. The PCBN coordinating center is at JHU. UW is a network site.

The Genitourinary Cancer Biorepository at the University of Washington joined the Prostate Cancer Pathology Resource Network (PCPN) September 30th 2014. The UW Prostate Cancer Program has for over 25 years collected and distributed biospecimens to investigators worldwide. During that time the University of Washington Biorepository has focused on advanced stage disease. Access to clinical specimens from patients with advanced disease can be challenging so the Genitourinary Cancer Biorepository set up a rapid autopsy program to provide access to metastatic tissue and create patient derived xenograft (PDX) models of advanced disease. The biorepository also has an extensive collection of blood (serum, plasma, and buffy coat), prostatectomy tissues (frozen), and derived specimens (DNA and RNA) from prostate cancer patients; these specimens are linked to clinical and outcome data and supported by an informatics infrastructure.

Keywords

Biorepository, prostate cancer, patient derived xenografts, rapid autopsy, biomarkers.

Accomplishments

The Major goals of the project were (1) patient accrual and biospecimen acquisition, (2) providing specimens to external investigators, and (3) improving biospecimen science.

Patient Accrual and Biospecimen Acquisition:

The adjacent table shows specimens prospectively accrued to the PCBN through the University of Washington during the 12 month period covered by this report. African American patients comprised only 2% of the patient specimens we accrued at UW. Increasing enrollment is an ongoing challenge for investigators at UW.

Biospecimen Acquisition October 2015 - September 2016	Total Specimens Collected
Serum	
Pre-RRP	128
Metastatic	74
Total	202
Tissue	
Prostatectomy	91
Metastatic Sites Sampled	75
Normal Sites Sampled	86
Metastatic Biopsy	0
Total	252

Radical prostatectomies: During the year we prepared frozen OCT embedded tissues from 91 prostatectomies. Thirty-five were from high risk patients (Gleason 8 and above), 31 were from medium risk (Gleason 7) and 24 were low risk (Gleason 6). One had an undetermined Gleason due to prior hormone and radiation treatment.

Rapid autopsies: We performed six rapid autopsies during the last year. The prostate cancer patients are approached by oncologists in the clinic and through the altruism and generosity of the patients and their families as soon as the patient passes we dispatch an ambulance to pick up the body and bring it back to the University of Washington where our autopsy team is prepared for a rapid autopsy and tissue acquisition. Based on our historic

data we typically expect 8 autopsies a year and we have performed 6 in the last year. All specimens have been processed and read by a pathologist.

Serum and Plasma Isolation: Sera were obtained from 128 prostatectomy patients and 74 metastatic patients. Plasma and buffy coats were obtained from 124 prostatectomy patients and 5 metastatic patients.

Metastatic Biopsies: We have obtained paraffin embedded metastatic biopsies from 0 patients. No oligo metastases or biopsies were available to the Biorepository for collection.

Tissue Microarrays: We have manufactured a PCBN specific metastasis TMA. The TMA consists of 1 bone and 1 visceral metastasis (where available) from each of 20 patients. This TMA is of the most recent rapid autopsies available – de-identified clinical data has also been abstracted. We are now in a position to create new TMAs with patients from the post-abiraterone/enzalutamide era and are designing the TMA.

Patient Derived Xenografts: We have implanted animals with tissue from 1 prostate cancer patient from the operating room, and 4 rapid autopsy patients. No new lines have been established this year based on the premise of the lines passaging over 3 times as xenografts in animals. We are currently maintaining 35 lines and continue to passage tumors in animals to develop new lines.

DNA/RNA Isolation: We have a bank of RNA from primary prostate, xenografts and metastases, but as we collect more tissue we isolate additional RNAs. This year RNA was isolated from a further 49 xenograft tumors (some in duplicate), and 16 additional metastases.

Providing Specimens to External Investigators:

We have provided serum samples from 70 patients with benign prostate, 70 Gleason 3+3, 70 Gleason 3+4, 70 Gleason 4+3, and 50 Gleason 8/9 to one investigator and serum from 20 castration-resistant prostate cancer (CRPC) and 20 control patients to another. RNA from LuCaP xenografts to one investigator and 20 RNA specimens from CRPC metastasis to another. One investigator received 4 xenograft TMAs and six investigators have received 14 metastases TMAs.

Improving Biospecimen Science:

Quality Assurance Study: In the past we have questioned whether the quality of RNA from rapid autopsy tissue was due to warm ischemia time or due to the pathology of the tumor (in some cases a significant amount of the tumor is necrotic). We are analyzing RNA specimens from the rapid autopsy program in an attempt to assess the impact of time on RNA quality. We have identified 90 specimens from 49 patients. We are cross referencing the tissue acquisition time, % necrosis in the tissue, tissue type and RIN to determine if there is a linear relation between time and RNA quality. Further, we have observed an increased number of patient specimens from the rapid autopsy program that appear to have lost androgen receptor expression. We are now starting to assess the specimens for androgen receptor, chromogranin A and synaptophysin expression to ‘phenotype’ the metastases.

Impact

No new PDX models were developed. Biospecimens from the clinic, operating room and at autopsy were collected for future use by the prostate cancer research community. Clinical specimens and associated data were provided to researchers.

Changes/Problems

As stated in the proposal we have made changes to our database, cleaning up data, increasing searchable fields, and transferring additional datasets into the database. We are in discussions with a group at the Fred Hutchinson

to switch over time to a new platform. Additionally, we have had two changes in personnel this year. Olena Tseona and Rebecca De Frates our two tissue acquisition personnel went on to a master's program and a research position in the Allen Institute for Brain Science respectively. They were replaced by Manix Poon and Halima Essien who are being trained by the Biorepository manager Lori Kollath and Dr. True (Pathologist).

Products

The reportable outcomes for the project include tissue acquisition, PDX development, and TMA construction, and specimen distribution are already discussed under accomplishments.

Participants & other Collaborating Organizations

This program involves interactions with the coordinating site at Johns Hopkins for the distribution of specimens.

Special Reporting Requirements

N/A

Appendices

N/A